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10/533,544	01/20/2006	Pierre Sevigny	074818.2	4538

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EXAMINER	
HOBBS, LISA JOE	
ART UNIT	PAPER NUMBER
1657	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/533,544	SEVIGNY ET AL.	
	Examiner	Art Unit	
	Lisa J. Hobbs	1657	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 August 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 3-12* is/are pending in the application.

4a) Of the above claim(s) *6-11* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 3-5, 12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim Status

Claims 1, 3-12 are active in the case. Claim 2 has been cancelled by preliminary amendment. Claims 1, 3-5 and 12 are under examination; claims 6-11 are withdrawn as drawn to a non-elected invention.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1 and 12, with dependent claims 3-5, are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. It is unclear what is intended by the phrase "a stabilizing amount" of a solubilizing agent. The metes and bounds of this claim are unclear. One of skill would not know the parameters of the word "stabilizing". For the purposes of this examination, the examiner has interpreted the claim to recite "the solvent which comprises at least one solubilizing agent selected from the group…"

Claims 1, 3-4 and 12 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential elements, such omission amounting to a gap between the elements. See MPEP § 2172.01. The omitted element is: a chromogenic substrate. The preamble recites that this composition is intended as a chromogenic substrate for detection of lacZ gene activity, but the composition, as recited, comprises:

1. At least one solubilizing agent selected from:
    a. NMP
    b. DMPU
    c. PC
2. Essential Oil

There is no element (3) that recites a chromogenic substrate capable of detecting lacZ gene activity or a chromogenic substrate selected from a group of particular substrates. The preamble is given limited patentable weight when interpreting the claim, since it merely recites an intended use, and the actual claim elements omit a chromogenic compound. The final phrase of the claim, that the elements result in a composition for detecting a lacZ gene activity, is not supported when there is no recitation of an element which is capable of detecting the gne activity.

Along with the rejection of the missing element in claims 1, 3-4, and 12 is a rejection of claim 5, which recites the limitation "said chromogenic substrate" in line 1. There is insufficient antecedent basis for this limitation in the claim since no chromogenic substrate is part of the composition of claim 1 as currently recited.

For the purposes of this examination, the examiner has interpreted the claims as reciting:

1. At least one solubilizing agent selected from the group consisting of:
    a. NMP;
    b. DMPU; and,
    c. PC;
2. Essential Oil;

3. At least one chromogenic substrate for detecting the presence of lacZ gene activity (with the following added in claim 5) selected from the group consisting of:

d. X-Gal; and,

e. IPTG.

Claims 1, 3-5 and 12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. It is unclear how a chromogenic substrate is able to detect the presence of a lacZ gene when there is no requirement that the gene be expressed or active. It is unclear from the specification, how one of skill would expect any chromogenic substrate of the instant invention, in composition additionally comprising a solubilizing agent and essential oil, to detect the presence of a DNA fragment. For the purposes of this examination, the examiner has interpreted the phrase to be "a chromogenic substrate for detecting the expression or non-expression of a lacZ gene".

Claim Rejections - 35 USC § 102

The rejection of claims 1, 3-5 under 35 U.S.C. 102(b) as being anticipated by Klopfenstein (EP 0354027 A3) is withdrawn in view of the arguments presented in applicant's response and the declaration submitted 12 August 2008; claim 2 was cancelled with the amendment of 12 August 2008.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 3-5 and 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Klopfenstein (EP 0354027 A3), Parham et al. (US 4596770 A), Dunn (EP 0950403 A3), and Mitchell et al. (WO 94/13777), in view of Gosnell et al. (US 2002/0086278 A) and Ward et al. (US 5403721 A).

A dipolar solvent is claimed for chromogenic substrate which comprises a stabilizing amount of at least one solubilizing agent selected from the group consisting of NMP, DMPU, and PC and comprises essential oil. Claim 4 recites a list of essential oil origins; claim 12 recites that the essential oil comprises about 1% to about 10%. Claim 5 recites that the chromogenic substrate is selected from the group consisting of X-Gal and IPTG.

Klopfenstein teaches a "biodegradable, non-toxic, non-hazardous solvent" (col. 1) comprising N-methylpyrrolidone and cyclic terpene (i.e., NMP and an essential oil comprising pine terpenoids), see for example, col. 10 and col. 11. Klopfenstein beneficially teaches that the above solvent has various uses, including dissolving inks in the silk screen and printing industries. Klopfenstein et al. teach that "the cyclic terpenes used in the solvent compositions are found in nearly all living plants and other organic products and are totally biodegradable. Consequently the solvent compositions of the present invention may be flushed with water into municipal sewer systems" (col. 1). Also, they teach it is "desirable to include in the composition emulsifiers and/or wetting agents…which fulfill their well known properties when used in

solvents of [this] type" and that "the addition of surfactant to the cyclic terpene mixture enhances the water rinsability of the solvent composition" (col. 4). As well, they teach that "the compositions…may be diluted with water, to form emulsions, prior to use for some purposes" (col. 6).

Parham et al. teach that "[i]t has now been found that in an enzyme immunoassay or enzyme-linked immunosorbent assay in which 3,3',5,5'-tetraalkyl benzidine chromogen or an acid salt thereof and a peroxide are reacted with a peroxidase in an aqueous buffered substrate medium, the step of providing the chromogen or acid salt in solution in an aqueous medium containing 5 to 20% by volume of N-methyl pyrrolidone (NMP) provides improved results in the form of increased stability of the substrate solution and decreased substrate drift as well as being free from biohazard and from toxicity" (col. 1). "The amount of N-methyl pyrrolidone present in the aqueous substrate mixture depends upon the concentration of the chromogen present; higher concentrations of chromogen require higher concentrations of NMP to solubilize the chromogen. In general, it is desired to minimize the concentration of NMP. It is found that the amount of NMP required to solubilize the chromogen is much less than the amount of 1,4-dioxane or of dimethyl sulfoxide required to solubilize the chromogen to the same extent. While concentrations of NMP from 5 to 20% by volume of the water may be used, it is preferred to use from 5 to 10% by volume. Excellent results are obtained using from 6 to 8% by volume when the concentration of the chromogen is of the order of 1-2 mM" and "[t]he determination of enzyme activity is carried out in the usual manner by incubating the substrate solution with the specimen containing the enzyme to develop a visible color. For quantitative determinations the reaction

with the substrate solution is stopped after an established time by adding a conventional stopping agent" (col. 2).

Dunn et al. teach "[a] composition…comprising: an emulsion or dispersion of a biologically active mixture… comprising [a] biologically active agent and a pharmaceutically acceptable oil…and a pharmaceutically acceptable organic solvent that is partially to completely soluble in the aqueous or body fluid" (claim 9), wherein the oil is an oil in an oil emulsion, the pharmaceutically acceptable oil is a plant oil, the pharmaceutically acceptable organic solvent is NMP or PC (claim 10). They teach that this composition is used for delivery of biological agents to patients and may comprise a range of biologically active compounds to be protected from dissolution or degradation in an aqueous solution and the solvent matrix can be manipulated as desired to increase or decrease water solubility (p. 8).

Mitchell et al. teach a cleaning composition comprising a dipolar aprotic or protic organic solvent, an aliphatic compound and a surfactant, wherein the preferred composition is in the form of a microemulsion. The preferred dipolar aprotic or protic organic solvent is N-alkylpyrrolidinone (especially N-methylpyrrolidonone) (abstract). They also teach that in addition to the dipolar compound, the aliphatic compound and the surfactant, the composition may comprise additives, for examples stabilizers (p. 6).

Gosnell et al. teach that in chromogenic assays "[a] small amount of the chromogenic substrate, from 0.05 to 0.2 g, preferably 0.05 to 0.1 g (e.g. 0.08 g) can be added to a small amount of DMSO (e.g. 1 ml.). Then a small aliquot of this solution (e.g. about 50 microliters) can be added to the surface of a pre-plated medium, either TSASB or chocolate agar, then distributed using a spreader." And, "[a]ll chromogens can be added aseptically to the base post

autoclaving at a preferred concentration of 0.1 g/l (a suitable range is 0.05 to 0.20 g/l). Chromogens are either pre-dissolved in DMSO or added as powder, if water soluble. Chromogens can also be added prior to autoclaving" [0046-7, esp. Tables III and IV]. Also, "[i]t was surprising to discover that chromogenic substrates dissolved in the organic solvent dimethylsulfoxide (DMSO), when applied to the surface of or incorporated within a highly colored medium (i.e., a medium containing blood or hemin) could support the growth of microorganisms and result in color differentiation of the microorganisms" [0071]. Both of the chromogenic compounds recited are included in Gosnell et al., who state that "X-gal was not particularly useful for Gram-positives. IPTG appeared to reduce the reactivity for some strains with X-gal. E. faecium (ATCC 49032) gave dark blue on X-Gal but no color on X-Gal with IPTG" [0102].

Ward et al. teach that "enzyme indicator device[s] may be made by dissolving a dye-forming substrate, such as X-Gal, in a solvent such as dimethylformamide (DMF), methyl cellosolve (2-methoxyethanol), or DMSO and mixing with a liquid polymer system, such as latex. Other adhesive-type polymers that can be dried into a solid or semisolid state include, for example, ethylene vinyl acetate (EVA), polyvinyl alcohol (PVA), and polyvinyl pyrrolidone (PVP). EVA is a polymer soluble in methylene chloride. Additionally, polymer systems that can be liquefied in solvents, such as methylene chloride are useful to liquefy the adhesive-type polymer for mixing with the dye-forming substrate. The mixture of dye-forming substrate and polymer is dried to form a solid or pliable solid. Preferably, the liquid dye-forming substrate and polymer, in a more viscous state, is layered onto the surface of a solid support. Most preferably, a solid support is a porous plastic material that can float on the surface of a liquid" (col. 10).

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to provide a stable, non-toxic organic solvent for a chromogenic susbtrate able to detect lacZ production, which solvent was in a microemulsion construction, based upon the teachings provided by Klopfenstein et al., Parham et al., Dunn et al., and Mitchell et al., who teach organic solvent compositions comprising NMP, PC and essential oils which compositions are taught to comprise chromogens, combined with the teachings of Gosnell et al. and Ward et al., who teach that lacZ product detection chromogens are well known by those of skill in the art to be effective when comprised within an organic solvent matrix. One of skill would be motivated to choose the best matrix for the desired assay, with special attention to the beneficial teachings of non-toxicity and ease of organic solvent disposal. From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention since many variations of organic solvents were known to those of skill and certain permutations, such as NMP combined with essential oils, were known to provide beneficial effects to the composition of X-Gal or IPTG in an organic solvent.

Response to Arguments

Applicant's arguments filed 12 August 2008 have been fully considered but they are not persuasive. Applicants argue that Klopfenstein et al. teach a cleaning solvent and do not teach a solvent that extends the stability over time of chromogenic substrates used in biological assays. This is correct, however, they teach that the components of the instant composition are known to be present in compositions together, are known to have various additives, and are known to

comprise water, if desired. Also, the claims do not recite a limitation that the composition is more stable over time. Applicants also argue that one of skill would not apply 80% cyclic terpene to a colorimetric composition. However, the amounts of terpenes, as taught in the various prior art documents, varies widely and it is taught that one of skill can choose the components and amounts to best suit the desired effect of the organic solvent compound: cell transformation, cleaning solvent, microemulsion with chromogens, etc.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lisa J. Hobbs whose telephone number is 571-272-3373. The examiner can normally be reached on Hotelling - Generally, 9-6 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon P. Weber can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Lisa J. Hobbs/
Primary Examiner
Art Unit 1657

ljh